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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/488,737	01/20/00	LISSOLO	L 50019/008001

HM22/0531

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1645	8

DATE MAILED: 05/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/488,737	Ling
Examiner	**Group Art Unit**
Portner	1645

☒ Responsive to communication(s) filed on *Dec 18, 2000* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-16* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-16 are pending.

Claim Objections

1. Claim 16 is objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must depend upon other claims in the alternative and it depends upon both claim 1 and claim 10. See MPEP § 608.01(n). Accordingly, claim 16 has not been further treated on the merits.

Specification

2. The disclosure is objected to because of the following informalities: At page 7, line 5, an amino acid sequence that falls within the sequence rule requirement is recited; it appears to be SEQ ID NO 1. Incorporation of a SEQ ID NO at this location, would place the sequence in compliance with the sequence rules.(see 37 CFR 1.821-1.825). .

Appropriate correction is required.

Brief Description of the Drawings

3. Brief Description of the Several Views of the Drawing(s) is recited at page 20, starting at line 21. A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74. Insertion of a header at this location would set forth this section of the specification

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7, 9, 11, 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed proteins of Helicobacter pylori and immunogenic fragments therefrom, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

The specification discloses several proteins which are substantially purified and is immunoreactive with an antisera raised thereto; the specification on page 7, lines 20-24 and page 8, lines 1-16 states that these proteins may be mutated at one or more amino acids by deletion, addition or substitution, no sequences either amino acid or nucleic acid are disclosed other than the N-terminal sequence of the 50 kDa antigen but this sequence does not define the active cite(s) of the 50 kDa protein or any of the other mutated proteins claimed. No specific guidance directing where changes could be tolerated that will not effect the over structure and function of the protein are described The claimed fragments and/or mutated protein need only be capable of reacting with an antisera, therefore claims encompass the deletion, substitution or

insertion of any combination thereof, therefore **any** amino acid is being claimed, and **no** specific location for where the deletion, substitution or insertion or any combination thereof within the mutated protein or fragment is recited. If all the amino acids are deleted or substituted or inserted the resulting synthetic peptide could result in a peptide not taught and enabled by the specification. No pharmaceutical compositions that comprise specific fragments that are able to treat or prevent Helicobacter infection are taught.

Thomas E. Creighton, in his book, "Proteins: Structures and Molecular Properties, 1984",(pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes:

1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; and

2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a Proline residue, which must distort the alpha-helix.

Thomas E. Creighton, in his book "Protein structure: A Practical Approach, 1989; pages 184-186" teaches that present day site directed mutagenesis of a gene allows any amino acid in a protein sequence to be changed to any other, as well as introducing deletions and insertions. The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph) adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differs from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

The substitution of **any** amino acid in **any** location within the protein would not predictably result in a stable molecule. Specific amino acids in specific locations which result in stable mutations are not taught. The specification does not provide guidance on how any amino acid can be deleted, substituted or inserted or any combination thereof for the production of a stable and active fragment with the functional characteristics of the native protein nor does the specification provide guidance on how any location can be used to produce a stable polypeptide. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which deletions, substitutions or insertions or any combination thereof would result in the desired product. Accordingly, one of skill in the art would be required to perform undue experimentation to use any amino acid at any location to produce a stable active protein. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation. In light of the fact that the mutant proteins of claims 7 and 9 are not so enabled that the person of skill in the art could make and use them, the claimed monospecific antibodies are also not enabled.

It would therefore require undue experimentation on the part of the skilled artisan to make polyclonal antibodies with the instantly claimed binding specificity to a protein or polypeptide that does not evidence original descriptive support which enables the production and isolation of monospecific antibodies to the mutant protein.

6. Claims 7-11, 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 7 recites the phrases: "by fragmentation and/or mutation" and "capable of being recognized by an antiserum raised against a protein". The phrase "a protein" lacks antecedent basis in claim 1. The size, nature and means of fragmentation are not clear; the claim as now written could encompass a single amino acid of the original polypeptide which has been fragmented. Therefore the recitation of the word "fragmentation" fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "capable of" has been held that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69, USPQ 138. This rejection could be obviated by amending the claim to recite --antigenic fragments-- or --immunogenic fragments-- or another phrase which is comparable to the suggested phrases above.

Claim 7: The phrase "and/or" does not clearly set forth the invention as it is not clear that the invention is a mutant fragment or a mutated protein or a fragment of the Helicobacter protein. Clarification is requested.

The type of mutation which still provides for antigenicity and recognition as an Helicobacter pylori protein is not clearly defined in the claims. Where or what type of mutation which would allow for alterations but still maintain the proteins antigenic nature is not clearly set forth, therefore the recitation of the word "mutation" fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. In claims 8-11, the phrase "a protein or a polypeptide lacks antecedent basis in claim from which they depend.

9. Claims 12 and 13 do not further limit the claim from which they depend and therefore does not distinctly claim Applicant's invention.

10.Claims 14-15 recite methods steps in the passive voice, this does not distinctly claim Applicant's invention. Amendment of the claim to recite positive steps could obviate this rejection.

Claim Rejections - 35 U.S.C. § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

12. Claims 1,3-4, 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Landini et al (1989).

The claimed invention is directed to Helicobacter pylori proteins of 32-35 and 30 kDa that are substantially purified, with an N-terminal of SEQ ID NO 1 and formulated into a pharmaceutical composition.

Landini et al disclose substantially purified Helicobacter pylori antigens, wherein the approximate molecular weight of two the isolated proteins were 34 and 28 kD and were considered to be Helicobacter pylori specific antigens. (See abstract, and Figure 2, page 186).

The antigens were substantially purified through electrophoresis in a 10% acrylamide gel into separated proteins (see page 183, col. 1, paragraph 2). The 28 kDa protein reads on the now claimed 30 kDa and the 34 kDa reads on the antigen of 32-35 kDa, as the disclosed relative

molecular weight value is within the acceptable range of variance when determining relative molecular weight by SDS-PAGE gel electrophoresis.

Landini obtained the antigen by a materially different process but the isolated and purified proteins of Landini appear to be the same or equivalent proteins to those now claimed and therefore anticipates the instantly claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

13. Claims 1-3,5-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Husson et al (1993).

The claimed invention is directed to Helicobacter pylori proteins of 54, 50, 32-35 and 30 kDa that are substantially purified and formulated into a pharmaceutical composition.

Husson et al disclose antigens which substantially purified Helicobacter pylori antigens which are capable of reacting with antibodies, wherein the approximate molecular weight of the isolated proteins were 57, 54 (a heat shock protein and therefore not immunoreactive with catalase), 52,48,45,37,33,30 and 29 kDa (see page 2697, column 1, paragraph 2) .

A composition of substantially purified Helicobacter pylori antigens that comprised a pharmaceutical carrier is disclosed . The pharmaceutical composition was obtained through fractionation, sonication, centrifugation, and resuspension in sterile distilled water. This composition was further purified using gel electrophoresis (see page 2695, col. 1, last paragraph and col. 2, first paragraph).

Husson obtained the substantially purified proteins of by a materially different process but they appear to be the same proteins now claimed and therefore anticipate the instantly claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

14. Claims 1-9,15 are rejected under 35 U.S.C. 102(e) as being anticipated by Calenoff (US Pat.5,567,594, filing date: December 20, 1993).

The claimed invention is directed to Helicobacter pylori proteins that are in substantially purified form, of relative molecular weights of 54, 50, 32-35 and 30 kDa, wherein the antigens have been formulated into a pharmaceutical composition, and one of the antigens has an N-terminal amino acid sequence of SEQ ID NO 1.

Calenoff discloses antigens which are substantially purified Helicobacter pylori antigens reactive with antibodies, wherein the approximate molecular weight of the isolated proteins were:(See columns 13-16)

53 kDa(designated 2.7.3)

51 kDa (designated 5.12.1), 49 kDa (designated 2.12.1), 48 kDa(designated 1.12.1)

34 kD (designated:2.12.1 and 3.12.3), 36 kDa(designated 8.12.2) and

31 kDa(designated 3.12.4 and 4.12.3), 29 kDa (designated 3.12.5).

The disclosed protein antigens read on the now claimed protein antigens of 54, 50, 32-35 and 30 kDa as the values are within the acceptable range of variance when determining relative molecular weight by SDS-PAGE gel electrophoresis and teaches the evaluation of the antigens to define epitope fragments of the antigens that are immunoreactive with patient antibodies (col. 18, lines 48-55).

The Helicobacter proteins or polypeptides are used in the formulation of pharmaceutical compositions that contain injectable liquid solutions or suspensions, to include emulsions and encapsulated liposomes (see col. 18, lines 47-67 and col. 19, lines 1-42), buffers, adjuvants saline, dextrose, glycerol, ethanol and combinations thereof.

Calenoff does not disclose an N-terminal amino acid sequence of SEQ ID NO 1, for the Helicobacter antigens, but the disclosed antigens would inherently evidence the recited SEQ ID No 1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious

difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

Antibodies specific for bacterial antigens are taught for the purification of antigens which contain epitopes immunologically identifiable with epitopes of Helicobacter pylori (see col. 19, lines 66-67 and col. 20, liens 1-11).

Calenoff obtained the antigens by a materially different process but the isolated and purified proteins of Calenoff appear to be the same proteins to those now claimed and teaches means and methods for the attainment of purified proteins.

Calenoff inherently anticipates the instantly claimed invention.

15. Claims 1,2,7-9,15 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferrero et al (1995).

The claimed invention is directed to Helicobacter pylori protein antigen of 54 kDa, wherein the protein is in substantially purified form, formulated into a pharmaceutical composition, is capable of reacting with antiserum raised to the protein and used in a immunological method of diagnosing Helicobacter through detection of antibody/antigen complexes formed between with diagnostic antibodies present in a biological sample and the 54 kDa antigen.

Ferrero et al disclose a Helicobacter pylori antigen of 54 kDa, in substantially purified form obtain from culture lysates through affinity and anion-exchange chromatography, and gel electrophoresis (see page 6499, col. 2, last paragraph and page 6500, col. 1, first paragraph).

Pharmaceutical compositions that comprised the 54 kDa Helicobacter antigen together with 0.1 M sodium bicarbonate were produced (see page 6500, col.. 1, paragraph 3, second to last sentence).

Two methods of detecting serum antibodies to the 54 kDa Helicobacter protein are disclosed, wherein the methods were immunoblotting and enzyme linked immunosorbent assay. The biological sample was contacted with the polypeptide and the immune complex formed between the serum antibodies and the polypeptide detected (see page 6500, col. 1, paragraphs 2; Figure 2, page 6501 and col. 2, paragraph 1, page 6501).

The disclosure anticipates the now claimed proteins with a relative molecular weight of about 54 kDa.

16. Claims 1,2, 10 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Leying et al (1992).

The claimed invention is directed to a composition of Helicobacter pylori substantially purified protein antigen of about 54 kDa and a method of detecting the antigen with monospecific antibodies produced to the antigen.

(Claims 1-2; Protein Composition) Leying et al disclose a Helicobacter pylori antigen of about 54 kDa, wherein the 54 kDa antigenic protein was determined to be a flagellin antigen (abstract, page 2863, col. 1; and page 2871, col. 2, paragraph 2).

(Claim 10, antibody composition) Monospecific antibodies obtained through immunization of rabbits with flagellar filaments purified by gel chromatography were used in a method of detecting Helicobacter pylori antigen (page 2872, col. 2, paragraph 4).

(Method claim 14) The detection method comprised the steps of contacting a biological sample with an antibody to form an immune complex. The presence of the polypeptide in the immune complex was detected through an alkaline phosphatase-coupled Protein-A system reagent (see page 2872, col. 2, paragraph 4).

The reference inherently anticipates the now claimed invention.

17. Claims 1,5,10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Bolin et al (1995).

The claimed invention is directed to a Helicobacter pylori 30 kDa protein in substantially purified form, a pharmaceutical composition that comprises the protein, antibodies to the protein and methods of detecting Helicobacter pylori 30 kDa antigen and antibodies immunoreactive with the 30 kDa antigen.

(Claims 1 and 5) Bolin discloses a Helicobacter pylori protein in substantially purified form of about 30 kDa (see page 383, Figure 1).

(Claims 10) Bolin et al show a monospecific, monoclonal antibody specific for an outer membrane antigen of 30 kDa of Helicobacter pylori (see page 383, Figure 1).

(Claim 11) The monoclonal antibody would be capable of recognizing a protein or polypeptide that evidences sequences present in a Helicobacter pylori fragment protein that contains that immunoreactive epitope to which the monoclonal antibody reacts. The monoclonal antibody would also be capable of reacting with a mutant protein or polypeptide, as the antibody need not specifically bind to the mutated region of the polypeptide but must only specifically bind to the protein of claim 1 because claim 7 defines the protein to be immunoreactive with antiserum raised against a protein of claim 1, which is not a mutant or fragment protein or polypeptide as recited in claim 7.

(Claim 12-13) A composition of the monoclonal antibody together with a pharmaceutical carrier was produced when the antibody was combined with phosphate buffered saline (PBS)-bovine serum albumin (BSA) and Tween was produced, as the recited intended use of a composition does not define over the prior art (see page 382, col. 1, first paragraph).

(Claim 14) A diagnostic method is disclosed that comprises reacting a monospecific monoclonal antibody with a biological sample to form a complex with intact bacteria in the sample. The

presence of an antibody/antigen complex was detected after unbound material was removed through incubation of the sample with a detection reagent (see page 381, col. 2, Dot blot test and SDS-PAGE and immunoblotting paragraphs 5-6; Figure 2, page 383; Figure 3, page 383, col. 2, top of page)

(Claim 15) The reference also discloses a method of detecting antibodies immunoreactive with a 30 kDa Helicobacter pylori antigen in a sample, wherein the sample is contacted with a 30 kDa Helicobacter polypeptide in substantially purified form and the immune complex formed between the antibody in the sample and the polypeptide was detected (see Figure 1, page 383, col. 1 and page 381, col. 2, paragraph 5).

The disclosure of the reference anticipates the now claimed invention.

18. Claims 1,3-5, 7, 8, 10-12 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Doig et al (1994).

The claimed invention is directed to Helicobacter pylori proteins in substantially purified form, pharmaceutical compositions that comprise the proteins and antibodies that are monospecific to the proteins.

(Claims 1, 3-5, 8) Doig et al disclose membrane proteins of 31, 48, 50 and 51 kDa which would not be immunoreactive with catalase antibodies, wherein the antigens were determined to have

other antigenic characteristics, wherein the values are within the acceptable range of variance (about 10% variation) when determining relative molecular weight by SDS-PAGE gel electrophoresis and read on the now claimed antigens of 30, 50 kDa (see page 4527, col. 1, paragraphs 3-4; page 4528, Table 1; page 4530, Figures 3-4).

Inherently the 50 kDa protein would evidence the N-terminal amino acid sequence claimed (claim 4).

(Claim 8) The antigens were used as pharmaceutical composition to stimulate an immune response in a mammalian host (see page 4527, col. 2, paragraphs 3 and 5).

(Claims 10-12) Monospecific, monoclonal antibodies were produced and found to be immunoreactive with 31, 48, 50, 51 and 60 kDa antigens (see material and methods section and Table 1, page 4528). Antibodies were diluted in a pharmaceutically acceptable carrier: 10mM Tris-HCL, 0.9% NaCl-0.05% Tween-20, pH 7.5 (see page 4528, col. 1, lines 1-2 and page 4527, col. 1, paragraph 5 (definition of TTBS provided))

(Claim 14) The reference discloses a method of detecting Helicobacter in a biological sample, wherein the monospecific antibody is contacted with a biological sample to form an immune complex with the Helicobacter pylori polypeptide to which is it specific. The complex is then detected (see page 4528, col. 1, paragraph 2 and page 4529, Figures 1 & 2).

(Claim 15) The reference discloses a method of detecting an anti-Helicobacter pylori antibody in a sample, wherein substantially purified antigens are separated by gel electrophoresis and electroblotting, then immunoreacted with a biological sample to detect the presence or absence of antibody contained therein. (see page 4527, col. 1, paragraph 3-4; Table 1 on page 4528; col. 2, paragraphs 2-4 and page 4529, col. 2, paragraphs 1-4; and page 4530, Figures 3 and 4).

The reference inherently anticipates the now claimed invention.

19. Claims 1-2,5-6, 8,10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Alemohammad (US Pat.5,262,156).

The claimed invention is directed to Helicobacter pylori antigens in substantially purified form, pharmaceutical compositions that comprise the antigens and antibodies immunoreactive to the antigens.

(Claims 1-2, 5-6) Alemohammad discloses an antigenic composition comprising substantially purified Helicobacter pylori antigens reactive with antibodies, wherein the approximate molecular weight of the isolated proteins were 31 kDa, 33 kDa (see column 2, Table 1 and col. 5, lines 1-23), as well as a 54 kDa antigen defined as a putative flagellin antigen(col. 2, line 36). The 54 kDa antigen would not immunoreact with catalase antibodies as it would have different immunoreactive epitopes.

(Claim 8) The antigens were in a pharmaceutically acceptable solution of phosphate buffered saline (see col. 6, lines 63-65; col. 7, line 40) thus defining a pharmaceutical composition containing the substantially purified Helicobacter antigens.

(Claims 10-11) Affinity purified antibodies to using Helicobacter antigens were produced (column 7, lines 40-55). These antibodies in turn were used as a control for a diagnostic method.

The substantially purified proteins of Alemohammad were obtained by a materially different process but they appear to be the same proteins now claimed and therefore anticipate the instantly claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

20. Claims 1-6, 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Pronovost et al (US Pat. 5,814,455 and 5,846,751).

The claimed invention is directed to Helicobacter pylori antigens in substantially purified from and used in a method of detecting antibodies in a biological sample.

Pronovost et al disclose Helicobacter pylori antigens of 29 kDa, 31 kDa, 45 kDa, 52 kDa, 56 kDa in substantially purified form (see all claims).

The disclosed antigens were used in a method of detecting antibodies in a biological sample, wherein the method was an enzyme linked immunosorbent assay, that detected the presence of polypeptide/ antibody complexes (see Example 4, col. 11-12)

Inherently the antigens disclosed correspond to, are the same antigens of about 30 kDa, 32 kDa, 50 kDa and 54 kDa because the relative molecular weights of the antigens in the prior art are within the acceptable range of variance (about 10%) when the molecular weight is determined by SDS-PAGE. The N-terminal sequence of the about 50 kDa antigen would be an inherent characteristic of the disclosed antigens of the prior art.

The reference anticipates the now claimed invention.

21. Claims 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Cordle et al (US Pat. 5,260,057).

The claimed invention is directed to monospecific antibodies to Helicobacter pylori antigens formulated into pharmaceutical compositions.

(Claims 10-13) Cordle et al disclose pharmaceutical compositions that comprise isolated and concentrated specific immunoglobulins for Helicobacter pylori surface membrane antigens (see col. 5, lines 41-46; Col.. 4, lines 8-63).

The reference anticipates the now claimed compositions which recite open language and permit the presence of other antibodies to other Helicobacter pylori antigens as the antibody compositions were raised to whole cell antigen compositions which would comprise all of the antigens present in Helicobacter pylori, to include the now claimed 30, 32-35, 50 and 54 kDa antigens..

22. Claims 10-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruiz et al (WO94/06474).

The claimed invention is directed to monospecific antibodies and pharmaceutical compositions that comprises the antibodies, wherein the antibodies are immunoreactive with Helicobacter pylori antigens, to include a 30 kDa antigen, and a method of detecting antibodies immunoreactive with Helicobacter antigens..

Ruiz et al disclose monospecific antibodies (see page 4, lines 27) directed to Helicobacter pylori outer membrane antigens and to Helicobacter urease (see Figure 4a and 4b) or immunogenic fragments thereof (see page 2, lines 33-37 and page 3, lines 9-12) , wherein the antibodies are combined with a pharmaceutically acceptable carrier such as water or saline (see page 3, lines 16-17; page 5, lines 30-33 and page 6, lines 1-33).

The reference teaches a method of detecting Helicobacter pylori antigen in a sample, wherein the monospecific antibodies are immobilized on a solid phase and reacted with a biological sample to form a complex (see page 8, lines 8-37 and page 9, lines 1-6)

The reference anticipates the now claimed compositions which recite open language and permit the presence of other antibodies to other Helicobacter pylori antigens.

Conclusion

This is a non-final action.

The following references are being cited and are duplicative of the references above, but would be applied to the claims if necessitated by amendment:

23. EP 484 148 (Ando et al) is cited to show affinity purification of antibodies to Helicobacter antigens.

24. Yokota et al (1994) is cited to show Helicobacter pylori antigens of 54 and 30 kDa (see page 405, Table 2, top of page).

25. Mizuta et al (1993, abstract).disclose substantially purified Helicobacter pylori antigens which evidenced a relative molecular weights of 33-35 kDa and 66 kDa in an immunoblotting immunological method.

26. Andersen et al (1995).disclose the isolation and purification of diagnostic low molecular weight Helicobacter pylori antigens, wherein one of the disclosed antigens is 30 kDa is substantially purified (See Figure 1, page 157, lane 2; abstract)

27. Dunn et al (1991) disclose a Helicobacter pylori antigen of 54 kDa in substantially purified form obtained through two dimensional electrophoresis.

28. Geis et al (1993) disclose Helicobacter pylori antigens of 53, 51, 49, 29.5 kDa. (see Figure 5, page 375).

29. Exner et al (1995) disclose the isolation and purification of Helicobacter pylori antigens of apparent molecular weights of 48, 49,and 50 (abstract; Material and Methods, pages 1567-1568; Figure 1, page 1568 col. 2).

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-~~0196~~ 1235.

Vgp
April 2, 2001

L. F. Smith

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